REMARKS

At the outset, it is noted that a shortened statutory response period of three (3) months was set in the November 5, 2007 Official Action. The initial due date for response, therefore, was February 5, 2008. A petition for a three (3) month extension of the response period is submitted with this amendment and request for reconsideration, which is being filed before the expiration of the three (3) month extension period.

It is also noted preliminarily that the restriction requirement set forth in the preceding Official Action has been made final. In accordance with the decision in *In re Ochia*, 37 USPQ 1127 (Fed. Cir. 1995) and *In re Brouwer*, 37 USPQ2d 1663 (Fed. Cir. 1966), and the Notice published in the Official Gazette on March 26, 1996, setting forth guidelines for the treatment of restricted product and process claims (see 1184 OG 86), applicants respectfully request that since this restriction requirement has been made final, in the event the claims of elected Group I (claims 1-4 and 11-23) are found allowable, then the method claims of Group II (claims 24-33) be rejoined and examined for patentability. See §821.04 of the Manual of Patent Examining Procedure (MPEP).

As another preliminary matter, applicants respectfully take exception to the examiner's statement that in the event claim 2 is found allowable, then claim 3 would be objected to as being a substantial duplicate of claim 2. Such an objection would be manifestly improper. Claim 2 recites 42 separate species of compounds that are encompassed by the genus of claim 1. Claim 3, on the other hand, recites only six specific compounds. It should be apparent that this is not a case in which two claims cover the same invention in slightly different words. Rather, the two claims in question differ substantially in scope. This, according to MPEP §706.03(k), is sufficient to preclude an objection based on duplicate claims.

Turning to the substantive aspects of the November 5, 2007 Official Action, claims 11-23 stand rejected for alleged failure to satisfy the enablement requirement of 35 USC §112, first paragraph. Applicants respectfully disagree with this ground of rejection, inasmuch as the present specification provides more than adequate guidance to allow the artisan of ordinary skill to administer the claimed compounds for the prevention of pneumovirus infection. Nevertheless, in the interest of advancing the prosecution of this application, and without acquiescing in the propriety of this rejection, claim 11 has been amended by deleting the words "or preventing". The deletion of this subject matter from claim 11 is without prejudice to applicants' right to file a divisional application with respect

to the deleted subject matter, as provided in 35 USC §120.

Claims 1-4 and 11-23 have been rejected under 35 USC §103(a), as allegedly unpatentable over WO 99/33508 of Nitz et al., considered in view of Avis, Pharm. Dosage Forms, Vol. 1: Parenteral Medications, 173-175 (1992). In support of this rejection, the examiner asserts that the claimed compounds are positional isomers of the compounds disclosed in WO 99/33508 and, as such, would have been obvious to the artisan of ordinary skill. Avis is cited for its disclosure of useful carrier vehicles for parenteral formulations. According to the examiner, it would have been obvious to one of ordinary skill in the art, at the time the present invention was made, to combine the disclosures of WO 99/33508 and Avis, because in doing so one purportedly would create a pharmaceutically active formulation suitable for safe administration to a patient. *In re Deuel*, 34 USPQ2d 1210, 1214 (Fed. Cir. 1995) is cited in support of this ground of rejection.

The foregoing rejections and provisional objection constitute all of the grounds set forth in the November 5, 2007 Official Action for refusing the present application.

No new matter has been introduced into this application by reason of the aforementioned claim amendment, entry of which is respectfully requested.

As a result of the present amendment of claim 11, the 35 USC §112, first paragraph, rejection of claims 11-23 has been overcome. Thus, the only matter remaining to be addressed is the rejection of claims 1-4 and 11-23 as allegedly obvious over the combined disclosures of WO 99/33508 and Avis. For the reasons given below, this ground of rejection is respectfully traversed.

In view of the recent opinion of the Court of Appeals for the Federal Circuit in *Takeda Chemical Industries Ltd. v. Alphapharm Pty. Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007), the 35 USC §103(a) rejection of claims 1-4 and 11-23 based on the combined disclosures of WO 99/33508 and Avis is plainly untenable and should, therefore, be withdrawn upon reconsideration.

In *Takeda*, the Court stated that a finding of *prima facie* obviousness of a chemical compound requires that the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention. The Court went on to comment in this regard, as follows:

> [I]n cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a

> particular manner to establish *prima facie* obviousness of a new claimed compound. *Id.* at 1174.

In rejecting the defendant's obviousness argument in *Takeda*, the Court adopted the District Court's finding that there was "nothing in the prior art to suggest making the specific molecular modifications to [the most closely related prior art compound] that are necessary to achieve the claimed compounds. *Id.* at 1177. The molecular differences between the compounds claimed by applicants herein and those of WO 99/33508 are at least as patentably significant as those found to exist in *Takeda* (5-{4-[2-(5-ethyl-2-pyridyl)ethoxy]benzyl}-2,4-thiazolidinedione vs. 5-{4-[2-(6-methyl-2-pyridyl)ethoxy]benzyl}-2,4-thiazolidinedione). Moreover, in the present case, just as in *Takeda*,. there is no disclosure in the cited prior art to suggest to an artisan of ordinary skill that meta versus para-substitution on the phenyl ring of the methylene bisphenol compounds called for in claim 1 would bring about a reasonable expectation of success.

Furthermore, the court reconciled its holding in *Takeda* with a number of prior decisions, including *In re Deuel, supra*. Specifically, the Court, in referring to *Deuel*, stated:

> We clarified, however, that in order to find a *prima facie* case of unpatentability in such instances, a showing that the "prior art would have suggested making the specific molecular modification necessary to achieve the claimed invention" was also required [citations omitted].

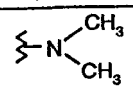
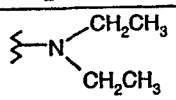
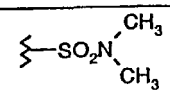
The examiner appears to have overlooked this particular passage of the *Deuel* opinion.

The argument advanced by the examiner in support of this rejection is untenable for the additional reason that the cited references fail to support the legal conclusion that the claimed compounds and method of use thereof are unpatentable according to the obviousness standard of 35 USC §103(a). It has long been held that a rejection under 35 USC §103 is proper only when the invention as a whole is shown to be obvious in view of the prior art. Moreover, since chemical compounds are inseparable from their properties, the properties of a claimed compound must also be considered as a part of the invention as a whole in assessing patentability under 35 USC §103(a). *In re Albrecht*, 185 USPQ 585 (CCPA 1975).

It is stated in the present specification that:

The compound of Formula I is useful for treating and preventing RSV disease and has improved solubility in pharmaceutical formulations. In particular, the compounds of Formula I have improved solubility in ethanolic solvents (see Table 2). The indicated improved solubility characteristics facilitate the preparation of pharmaceutical formulations and the delivery of the pharmaceutical formulations to a patient's pulmonary system using electrohydrodynamic (EHD) technology. Electrohydrodynamic spraying is a known process whereby solutions are aerosolized using electrical forces. In an EHD spray nozzle, the fluid to be aerosolized flows over a region of high electric field strength and receives a net electrical charge that remains on the surface of the fluid. As the solution exits the nozzle, the repelling force of the surface charge generates a thin jet of fluid. The jet breaks up into droplets of uniform size that collectively form a cloud. The result in an aerosolized solution having a monodispersed particle size distribution and near zero velocity. The improved solubility of the compound of Formula I in the formulations used in an EHD device facilitates the delivery of higher concentrations of the desired compound to the patient pulmonary tissue with fewer numbers of actuations of the EHD device.

Table 2, referred to in the foregoing passage, includes the following data:

Example Number	R_1	Meta Position Solubility (mg/ml)	Para Position Solubility (mg/ml)
1	$-CH_2CH_2CH_3$	1.9	0.18
2		2.10	0.09
6	$-OCH_2CH_3$	1.85	0.30
16	$-CH_2CH_2OCH_3$	1.14	0.29
20		1.45	0.21
27	$-NO_2$	0.98	0.16
31		0.08	0.03

Applicants consider it not only unexpected, but, indeed, quite surprising that the solubility characteristics of the meta-substituted compounds claimed in claims 1-4 are so dramatically improved.

The improved solubility characteristics of the meta-substituted compounds of the present invention, as compared to the compounds disclosed in WO 99/33508 that are substituted at the para-position, could not have been predicted. This improved

solubility in the formulations listed in Table 2 was certainly not predictable from the water solubility of the respective position isomers, which is essentially similar. Moreover, the consequences of such an unexpected improvement in solubility in the ETOH:PG:H_2O formulation are therapeutically significant. Specifically, the para-substituted compounds of WO 99/33508 are only poorly soluble in the ETOH:PG:H_2O formulation of the type utilized for EHD delivery of pulmonary drugs. For example, the compound of Example 1 in WO 99/33508 is stably soluble in the formulation at 200 μg/mL, thus limiting the deliverable quantity of drug to approximately 4 μg per actuation of the device. This is about 10 times less than the anticipated therapeutic dose, and so would require 10 actuations of the device to deliver the desired dose. This is plainly impractical and would result in low patient compliance, thereby reducing the clinical benefit. The surprising improvement in solubility in the ETOH:PG:H_2O formulation observed for the meta-substituted compounds of the present invention, by contrast, allows for a single actuation to deliver the desired therapeutic dose.

The evidence of surprising and unexpected results presented by applicants herein must be considered in reaching a determination as to whether the claimed invention as a whole would have been obvious under 35 USC §103. *In re Margolis*, 228 USPQ 940 (Fed. Cir. 1986). The examiner has not given any indication that this evidence has been duly considered.

The artisan of ordinary skill would not find in Avis any useful guidance that pertains to pneumovirus drug formulations for delivery by inhalation, and certainly not the advantage to be gained in this connection by administering the meta-substituted comounds of the present invention, as compared to the para-substituted compounds of WO 99/33508. Avis teaches only general principles concerning one particular mode of parenteral drug delivery, i.e., drug preparations for administration by hypodermic injection.

In reconsidering this application, the examiner is requested to bear in mind that granting a patent on applicants' invention will in no way diminish the availability of pneumovirus treatments available to the public. The claims of this application would not preclude public access to the compounds described in WO 99/33508 administered in the manner described therein. Nor do the claims presented herein preclude utilization of the compounds described in WO 99/33508 when formulated

according to the teaching of Avis. Applicants' claims 1-4 and 11-23 cover only their particular meta-substituted compounds and their use in treating pneumovirus infection.

Lastly, the examiner is correct in presuming (at page 5 of the November 5, 2007 Official Action) that the subject matter of the various claims was commonly owned at the time the inventions covered thereby were made.

In view of present amendment and the foregoing remarks, it is respectfully urged that the rejections and provisional objection set forth in the November 5, 2007 Official Action be withdrawn and that this application be passed to issue, and such action is earnestly solicited.

Respectfully submitted,

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